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(54) Title of the Invention Skin Cosmetic

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Specification

1. Title of the Invention
Skin Cosmetic

2. Claims

(1) A skin cosmetic characterized in comprising one or two or more compounds selected from a group comprising cholesteryl sulfate and salts thereof.

(2) The skin cosmetic according to claim (1), containing 0.01-5 wt.% of cholesteryl sulfate and/or salts thereof.

The present invention relates to a novel skin cosmetic that promotes the moisture retention function of the skin, comprising one or two or more compounds selected from a group comprising cholesteryl sulfate (hereinafter abbreviated CHS) and salts thereof.

In the past, in order to maintain healthy skin, skin cosmetics had been compounded by including water-based skin moisturizers and oil-based skin softeners that give the skin the proper amounts of moisture and oils.

The skin moisturizers used include glycerin, propylene glycol, polyethylene glycol, pyrrolidone carboxylic acid and

others, but these may cause the stratum corneum of the epidermis (the outermost layer of the skin) to absorb moisture, and may conversely cause a loss of moisture from the skin, and also, skin cosmetics that contain large amounts of them may give a sticky feel, so they had not necessarily been satisfactory.

In addition, the skin softeners used include liquid paraffin, Vaseline, olive oil, Scwaran lanolin, synthetic ester oils and the like, but these also, when included in a skin cosmetic in amounts sufficient to prevent the transpiration of moisture from the skin, may cause blockage of the normal metabolism of the skin, among other disadvantages.

In consideration of the aforementioned disadvantage seen in skin softeners, the present inventors conducted diligent studies with the object of providing a skin cosmetic that, rather than merely depending on such mechanisms as supplying moisture to the skin or preventing the transpiration of moisture from the skin by the physical action of these compounds, would promote the moisture retention function that the skin was originally provided with, and keep the skin in a healthy state, or repair the skin to that state.

As a result, they found that this object is achieved by skin cosmetics that contain CHS and/or a salt thereof, thereby achieving the present invention.

To wit, the present invention is a skin cosmetic characterized in comprising one or two or more compounds selected from a group comprising CHS and salts thereof.

Moisture in the skin constantly travels from the interior of the skin toward the outer layers, in accordance with the gradient in the moisture content which decreases as one goes from the dermis toward the outer layers in the epidermis, comprising the basal cell layer and further the stratum corneum, and the moisture is ultimately transpired through the stratum corneum, but this transpiration of moisture is controlled by means of the protective function (barrier function) mainly formed from the dense cell structure of the stratum corneum. The amount of this transpiration [the insensible perspiration (transepidermal water loss) value (hereinafter referred to as the "TWL value")] may fall within the range of 0.2–0.3 mg/cm²/hr at the epidermis of the forearm, for example, with healthy skin in the normal state, and normally it is kept below roughly 0.25 mg/cm²/hr. In contrast, in the xeroderma (dry skin) states often seen, or in dry skin seen with aging skin, the TWL value may exhibit a value near the upper limit of the aforementioned range or even a larger value, thus confirming the fact that the moisture retention function of the skin is decreased and this derives from, in the case of these kinds of dry skin, it is in the state in which the normal control limit due to the protection function has been exceeded, or this protection function is exhausted.

Accordingly, if it is possible to make the cell structure of the stratum corneum more dense and thus activate this protective function, this will promote the skin's water retention function and thus the skin will be kept in a healthy state and also, moreover it will be possible to ameliorate or repair dry skin, and as a result of the studies of the present inventors, it became clear that a skin cosmetic that contains CHS and/or salts thereof normalizes these intercellular functions of the skin and makes the structure of the corneal cells denser so that the moisture retention function of the skin can be promoted.

For this reason, the present invention provides a skin cosmetic that, by promoting the moisture retention function of the skin itself, can ameliorate the dry skin condition, or keep the skin in the healthy condition and prevent its aging, and thus give the skin moistness (silky feel), flexibility (smooth feel) elasticity and glow.

In addition, in the case of the skin cosmetic according to the present invention, there is no need to use large amounts of moisturizers and softeners as in conventional skin cosmetics, so there is no risk of these compounds impeding the normal physiological functions of the skin.

In order to obtain the CHS and salts thereof to be used in the skin cosmetic according to the present invention, it is sufficient to use known methods, to wit, by dissolving cholesterol in formamide, dimethyl formamide, pyridine or other basic organic solvents, or in benzene, toluene or other organic solvents, and then reacting with anhydrous sulfuric acid, fuming sulfuric acid, chlorosulfonic acid, a pyridine-anhydrous sulfuric acid complex or other sulfuric acid esterifying agent, and the impure CHS thus obtained may be used as is, or in the form of a desired salt obtained by allowing various bases to act thereupon, and thus produced by the ordinary methods of fractional precipitation and manipulation using methanol, acetone, benzene, petroleum ether, purified water and the like.

Here, the usable salts of CHS include any of those that can be stably incorporated within a skin cosmetic base and that are harmless from a physiological standpoint, but to present several columns that are particularly preferable, these include, for example, as inorganic salts: sodium salt, calcium salt, magnesium salt, etc. and as salts with organic bases: lysine salts, aspartates, triethanol amine salts and the like. In addition, these salts may include, for sodium salts for example, the dihydrate or hexahydrate forms, with hydrates in various forms, and naturally these may be similarly used. Note that Table 1 presents examples of the CHS and salts thereof.

Table 1

CHS and Salts Thereof	Rational Formula	Melting or Decomposition Point (°C)
CHS	C ₂₇ H ₄₅ SO ₄ H	72–74
Sodium salt (dihydrate)	C ₂₇ H ₄₅ SO ₄ Na·2H ₂ O	163–167
Potassium salt (monohydrate)	C ₂₇ H ₄₅ SO ₄ K·H ₂ O	202–208
Calcium salt	(C ₂₇ H ₄₅ SO ₄) ₂ Ca	134–138
Magnesium salt	(C ₂₇ H ₄₅ SO ₄) ₂ Mg	137–143

With the present invention, CHS or salts thereof are incorporated into a skin cosmetic base as a single salt or a mixture of two or more salts. In addition, depending on the case, it is also possible to use CHS which is partially neutralized with an equal amount or less of a base.

The content of the CHS or salts thereof incorporated, as the total content of the one or two or more compounds thereof is typically in the range 0.01–5 wt.% of the total weight of the skin cosmetic, and preferably in the range 0.05–3 wt.%. If the content is less than 0.01 wt.%, the meritorious effect of the skin cosmetic according to the present invention will not be adequately achieved, and on the other hand if the content is in excess of 10 wt.%, there is no prospect for any further increase in the meritorious effect concomitant to the amount of increase.

The skin cosmetic according to the present invention containing this CHS and/or salts thereof may be manufactured by normal methods. To wit, it is sufficient to dissolve, disperse or uniformly mix one or two or more compounds selected from the group comprising CHS and the salts thereof into a desired skin cosmetic base, thus obtaining a lotion, milky lotion, cream or pack.

In this case, it is preferable for the sodium salts, potassium salts, lysine salts, triethanol amine salts or other salts of CHS to be uniformly mixed as an aqueous solution, while the CHS and the calcium salts, magnesium salts, aspartates and other salts thereof to be uniformly dissolved or dispersed in an oil-based base.

Here follows a detailed description of the present invention made with reference to working examples and experimental examples thereof.

Note that the method of measuring and the method of evaluating the *TWL* value, percentage change in the *TWL* value and exfoliation characteristics of corneal cells are presented below.

(1) *TWL* Value

We used a method whereby the change in the humidity of a sealed volume of air above the skin is measured using its electrical resistance.

To wit, we sealed a measurement cell to the skin of the experimental subject, forced dry air through the cell and thus adequately replaced the air within the cell with dry air, and then halted the supply of dry air and found the relative humidity within the cell at that time as RH_s (%), left the cell alone for 10 minutes and again measured the relative humidity within the cell as RH_{10} (%). The *TWL* value was calculated from the change in humidity values at this time by the following formula:

$$TWL = \frac{(RH_{10} - RH_s) \times D_r \times V \times 6}{S} \text{ (mg/cm}^2\text{/hr)}$$

Where,

D_r : density of saturated water vapor in air at the measured temperature (mg/L)

V : volume of the cell (L)

S : surface area measured (cm²)

(2) Percentage Change in *TWL* Value

We measured the *TWL* value before and after applying a sample (skin cosmetic) to the skin and calculated the percentage change therein by the following formula:

$$\text{Percentage change in } TWL = \frac{TWL_A - TWL_B}{TWL_B} \times 100(\%)$$

Where,

TWL_A : *TWL* value before application of sample (skin cosmetic)

TWL_B : *TWL* value after application of sample (skin cosmetic)

(3) Exfoliation Property of Corneal Cells

We applied Scotch tape (Nichiban mending tape) to the skin, removed the tape and thus caused corneal cells of the skin to be adhered to the tape. Next, we performed a detailed observation of the state of these corneal cells using a scanning electron microscope and, based on the criteria presented in Table 2, found an index value after determining the appropriate category for the exfoliation property of the corneal cells.

Table 2

State of Exfoliated Corneal Cells	Index Value
No scales found	1
Scattered small scales found	2
Scattered small to medium scales found	3
Conspicuous small to medium scales found	4
Conspicuous large scales found	5

Note that the exfoliation property of these corneal cells becomes an index for determining the structure of the stratum corneum, and typically in dry skin and aged skin, it is thought that the amount of intercellular binding is thought to be weak, and the density of its structure is low, so this index value is thought to increase.

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Working Examples 1–4 and Comparative Example 1 (Skin Cream)

(1) Composition

Ingredients	Content (wt.%)				
	Comparative Example	Working Examples			
		1	1	2	3
(A) { Beeswax Stearic acid Stearyl alcohol Reduced Lanolin Scwaran Sorbitan monostearate Polyoxyethylene sorbitan monostearate CHS Calcium salt of CHS Sodium salt of CHS (dihydrate)	2.0	2.0	2.0	2.0	2.0
	5.0	5.0	5.0	5.0	5.0
	3.0	3.0	3.0	3.0	3.0
	2.0	2.0	2.0	2.0	2.0
	15.0	15.0	15.0	15.0	15.0
	3.0	3.0	3.0	3.0	3.0
	3.0	3.0	3.0	3.0	3.0
	0.5		0.5		
				0.5	
					0.5
(B) { Lysine salt of CHS Propylene glycol Preservative					0.5
	5.0	5.0	5.0	5.0	5.0
	0.2	0.2	0.2	0.2	0.2
(C) { Purified water Perfume	61.75	61.25	61.25	61.25	61.25
	0.05	0.05	0.05	0.05	0.05

(2) Method of Preparation

Component (A) and component (B) were melted by heating each to 80°C, and then were cooled while stirring, and component (C) was added when they reached 50°C; stirring was continued until 30°C was reached, thus obtaining creams of each.

Experimental Example 1

We examined the *TWL* values of Comparative Example 1 and Working Example 1 of the present invention, and the effects they have on the corneal cell exfoliation property.

(1) Test Method

We assembled Group A as 20 test subjects (women in the age range of 20–25 years) that have normal healthy skin, Group B as 20 test subjects (women in the age range of 20–25 years) that exhibit normal dry skin, and Group C as 20 test subjects (women in the age range of 50–60 years) that exhibit dry skin due to aging, and measured the *TWL* value of the forearm skin of each subject in advance.

Next, all of the test subjects in Groups A, B and C were asked to apply the skin cream of Comparative Example 1 to the skin of their left forearm, and the skin cream of Working Example 1 of their right forearm twice daily (morning,

evening), continuously for one month. On the next day after the final application, the *TWL* values of all test subjects' left and right forearms where the cream had been applied were measured, and moreover the corneal cell exfoliation property thereof was also evaluated.

Note that as a result of examinations performed by physicians after the end of the application test, there were no abnormalities found with respect to the forearm skin or health of any of the test subjects.

(2) Results

Table 3 presents the *TWL* values before and after application of skin cream (average values of the 20 test subjects in each Group), the percentage change in the *TWL* value found from these *TWL* values, along with the index values for the corneal cell exfoliation property (average values of the 20 test subjects in each Group).

Note that in Table 3, the *TWL* values prior to applying cream increased in Group A, Group B and Group C in this order, and this indicates that the loss of moisture from the skin increases in this order, and so the density and function of the corneal cells decreases concomitantly.

Table 3

Test Subjects and Forearm Locations	Sample Applied	<i>TWL</i> Value (mg/cm ² /hr)		Percentage change in <i>TWL</i> value (%)	Corneal Cell Exfoliation Property
		Before Applying Cream	After Applying Cream		
Group A Healthy skin (20 subjects)	Left Comparative Example 1	0.230	0.225	2.2	1.7
	Right Working Example 1	0.240	0.220	8.3	1.4
Group B Dry skin (20 subjects)	Left Comparative Example 1	0.300	0.282	6.0	2.7
	Right Working Example 1	0.310	0.211	31.9	1.8
Group C Age-deteriorated skin (20 subjects)	Left Comparative Example 1	0.515	0.475	7.8	3.6
	Right Working Example 1	0.530	0.290	45.3	2.1

Based on the results illustrated in Table 3 the meritorious effects of the skin cream of Working Example 1 of the present invention were confirmed as follows.

(1) On the normal healthy skin in Group A, the moisture retention function of the original skin and the structural characteristics of the corneal cells were kept in the normal

state, so the effect of applying the skin cream according to the present invention (Working Example 1) is not readily evident, but still there was slight improvement in comparison to Comparative Example 1.

(2) On the dry skin of Groups B and C, there was a marked improvement in the *TWL* value of the right forearm ...

... skin where the skin cream according to the present invention (Working Example 1) was applied, in comparison to the left forearm skin (where the skin cream of Comparative Example 1 was applied), and the value thereof was equal to or close to that of normal skin. In addition, the skin cream according to the present invention was slightly better with respect to the corneal cell exfoliation property also.

To wit, the skin cream according to Working Example 1 of the present invention exhibited the meritorious effect of maintaining healthy skin in Group A, and in Groups B and C, it clearly had a meritorious effect of bringing it closer to healthy skin.

Based on these results, one can see that the CHS contained in the skin cream according to Working Example 1 of the present invention effectively acted on the cells in the stratum corneum, thus improving the intercellular binding ability in the stratum corneum and making its structure denser, thereby activating the protective function of the stratum corneum and promoting the moisture retention function of the skin, and yet it is still highly safe without impairing the physiological functions of healthy skin.

Experimental Example 2

We examined the change in the *TWL* values when the skin creams according to Working Examples 2, 3 and 4 of the present invention as well as the skin cream according to Comparative Example 1 were applied to dry skin.

(1) Test Method

We assembled 60 new test subjects that exhibited normal dry skin (women in the age range of 26–34 years) and divided them into three groups (Groups D, E and F). Prior to the start of testing, we measured the *TWL* value of the left and right forearm skin of all test subjects, and calculated the average value for each Group.

Next, all of the test subjects in Groups A, B and C were asked to apply the skin cream of Comparative Example 1 to the skin of their left forearm, and a different skin cream for each Group to the skin of their right forearm twice daily (morning, evening), continuously for one month, with Group D applying the skin cream of Working Example 2, Group E applying that of Working Example 3 and Group F applying that of Working Example 4, respectively. On the next day after the final application, the *TWL* values of all test subjects' left and right forearms where the cream had been applied were measured.

Note that as a result of examinations performed by physicians after the end of the application test, there were no abnormalities found with respect to the forearm skin or health of any of the test subjects.

(2) Results

Table 4 presents the *TWL* values before and after application of skin cream (average values of the 20 test subjects in each Group) and the percentage change in the *TWL* value found from these *TWL* values.

Table 4

Test Subjects and Forearm Locations		Sample Applied	<i>TWL</i> Value (mg/cm ² /hr)		Percentage change in <i>TWL</i> value (%)
			Before Applying Cream	After Applying Cream	
Group D (20 subjects)	Left	Comparative Example 1	0.290	0.273	5.8
	Right	Working Example 2	0.310	0.226	27.1
Group E (20 subjects)	Left	Comparative Example 1	0.295	0.283	4.1
	Right	Working Example 3	0.284	0.202	29.0
Group C (20 subjects)	Left	Comparative Example 1	0.305	0.281	7.9
	Right	Working Example 4	0.308	0.203	34.1

With the results presented in Table 4, we confirmed that the cream containing sodium salt of CHS, potassium salt of CHS and lysine salt of CHS in Working Examples 2–4 reduced the *TWL* values in the same manner as the skin cream containing CHS in Working Example 1, normalized the protective function of the stratum corneum and also promoted the moisture retention function of the skin.

Experimental Example 3

We assembled groups of 30 test subjects each (women in the age range of 26–34 years) that complained of dry skin and asked them to apply the skin creams of Comparative Example

1 and Working Examples 1–4 twice daily (morning, evening) continuously for one month. As a result of examinations performed by physicians after the end of the application test, there were no abnormalities found with respect to the forearm skin or health of any of the test subjects.

Table 5 presents the results of interviewing all test subjects in regard to the meritorious effects of giving skin moistness (silky feel), flexibility (smooth feel), elasticity and glow after applying the cream.

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Table 5

Item	Evaluation	Samples Applied				
		Comparative Example 1	Working Examples			
			1	2	3	4
Skin moistness	Extremely good	0 replies	19 replies	18 replies	19 replies	17 replies
	Good	3	6	10	5	6
	Somewhat good	6	3	2	4	4
	No change	20	2	0	2	3
	Somewhat poor	1	0	0	0	0
Flexibility	Extremely good	0	18	19	16	17
	Good	6	5	6	5	5
	Somewhat good	5	5	5	5	4
	No change	19	4	2	4	4
	Somewhat poor	0	0	0	0	0
Elasticity	Extremely good	0	15	16	19	18
	Good	1	7	5	6	7
	Somewhat good	4	5	6	4	3
	No change	24	3	3	1	2
	Somewhat poor	1	0	0	0	0
Glow	Extremely good	0	18	18	20	17
	Good	2	8	6	4	6
	Somewhat good	6	3	4	5	5
	No change	22	1	2	1	2
	Somewhat poor	0	0	0	0	0

As is evident from the results of Table 5, the skin creams of Working Examples 1–4 which contain CHS and salts thereof demonstrated effects that were markedly superior to the skin cream according to Comparative Example 1. Working Examples 5–8 and Comparative Example 2 (Skin Lotions)

We prepared a skin lotion (Comparative Example 2) according to the ordinary method using the following as the raw ingredients: 10 wt.% of ethanol, 3 wt.% of glycerin,

0.2 wt.% of polyoxyethylene sorbitan monostearate (solubilizer), 0.01 wt.% of preservative, 0.01 wt.% of perfume, artificial color and added purified water in the remaining amount to reach 100 wt.%. Next, we similarly prepared skin lotions (Working Examples 5–8) using the same raw ingredients as for Comparative Example 2, but adding sodium salt of CHS (dihydride) in the amounts indicated in Table 6 to reach 100 wt.%.

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Table 6

Comparative Examples and Working Examples	Content of Sodium Salt of CHS (dihydride) (wt.%)
Comparative Example 2	0
Working Example 5	0.01
Working Example 6	1.0
Working Example 7	3.0
Working Example 8	5.0

Experimental Example 4

We assembled groups of 30 test subjects each (women in the age range of 26–34 years) that complained of dry skin and asked them to apply the skin lotions of Comparative Example 2 and Working Examples 5–8 twice daily (morning, evening) continuously for one month. As a result of examinations performed by physicians after the end of the application test,

there were no abnormalities found with respect to the forearm skin or health of any of the test subjects.

Table 7 presents the results of interviewing all test subjects in regard to the meritorious effects of giving skin moistness (silky feel), flexibility (smooth feel), elasticity and glow after applying the cream.

Table 7

Item	Evaluation	Samples Applied				
		Comparative Example 2	Working Examples			
			5	6	7	8
Skin moistness	Extremely good	0 replies	0 replies	11 replies	23 replies	24 replies
	Good	1	7	9	5	5
	Somewhat good	3	13	7	2	1
	No change	23	10	3	0	0
	Somewhat poor	3	0	0	0	0
Flexibility	Extremely good	0	0	10	16	16
	Good	0	5	8	11	12
	Somewhat good	4	16	8	3	2
	No change	24	8	4	0	0
	Somewhat poor	2	1	0	0	0
Elasticity	Extremely good	0	0	12	21	22
	Good	0	6	9	7	7
	Somewhat good	3	15	6	2	1
	No change	23	7	3	0	0
	Somewhat poor	4	2	0	0	0
Glow	Extremely good	0	0	13	22	21
	Good	0	7	8	6	7
	Somewhat good	6	16	7	1	2
	No change	21	6	2	1	0
	Somewhat poor	3	1	0	0	0

As is evident from the results of Table 7, each of the skin lotions according to Working Examples 5–8 of the present invention demonstrated effects that were superior to those of Comparative Example 2, and particularly superior skin improvement effects were observed in the case of the skin lotions of Comparative Examples 6–8 in particular.

Note that the skin lotion of Working Example 8 exhibited a slight tendency to gel in long-term storage. Working Example 9 and Comparative Example 5 (Skin Packs (Membrane Type))

We prepared a skin pack (membrane type) (Comparative Example 3) according to the ordinary method using the following as the raw ingredients: 10 wt.% of polyvinyl alcohol (average degree of polymerization: 1750, degree of saponification: 88 mol%), 3 wt.% of glycerin, 0.02 wt.% of perfume, 0.05 wt.% of preservative, artificial color and added purified water in the remaining amount to reach 100 wt.%. Next, we similarly prepared a skin pack (membrane type) (Working Example 9) using the same raw ingredients as for Comparative Example 3, but adding 0.2 wt.% of a salt

prepared by neutralizing CHS in triethanol amine to pH=7.0 to reach 100 wt.%.

Experimental Example 5

We assembled groups of 50 test subjects each (women in the age range of 20–60 years) and asked them to apply the skin packs of Comparative Example 3 and Working Example 9 twice daily (morning, evening) continuously for one month. As a result of examinations performed by physicians after the end of the application test, there were no abnormalities found with respect to the forearm skin or health of any of the test subjects.

We interviewed all test subjects in regard to the meritorious effects of giving skin moistness (silky feel), flexibility (smooth feel), elasticity and glow after applying the skin packs (membrane type), and the numbers of subjects that replied to the effect that improvements occurred are presented in Table 8. The skin pack (membrane type) according to Working Example 9 was found to have clearly markedly superior meritorious effects in comparison to that of Comparative Example 3.

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Table 8

Item	Comparative Example 3	Working Example 9
Number of subjects with improved moistness	11 out of 50	41 out of 50
Number of subjects with improved flexibility	8 out of 50	36 out of 50
Number of subjects with improved elasticity	4 out of 50	33 out of 50
Number of subjects with improved glow	3 out of 50	36 out of 50

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